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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/822,860	04/13/2004	Koichi Matsuzaki	040176	2658

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WASHINGTON, DC 20006

EXAMINER

REDDIG, PETER J

ART UNIT	PAPER NUMBER
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1642

MAIL DATE	DELIVERY MODE
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05/17/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/822,860	Applicant(s) MATSUZAKI ET AL.	
	Examiner Peter J. Reddig	Art Unit 1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 09 March 2007.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) 6-12 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5, 13 and 14 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

1. The Amendment filed March 9, 2007 in response to the Office Action of December 14, 2006 is acknowledged and has been entered. Claims 1, 2, 4 and 5 have been amended and new claim 13 and 14 have been added. Claims 6-12 were previously withdrawn as drawn to a non-elected invention.

2. Regarding the restriction between Groups VIII to XIII.

Applicants' cites the statement from section 5 of the Office Action of December 14, 2006 indicating Groups VIII to XIII will be rejoined as drawn to a method for assessing the activity of fibrosis stimulating signal in hepatic fibrosis and the efficacy of the molecular targeting therapy for hepatic-fibrosis, but will remain restricted to three Groups of methods using antibodies specific for the phosphorylated linker region in Smad2, Smad3, or Smad2 and Smad3.

Applicant argues that Groups VIII to XIII all include only claim 11, yet the Examiner has withdrawn claim 11 from consideration. Applicant argues that, based on the Examiner's statement, claim 11 should be rejoined and at least some portion of its scope considered.

Applicants' arguments have been considered, but has not been found persuasive because section 5 does not state that Groups VIII to XIII will be rejoined to groups that do not recite claim 11 listed in the restriction of September 6, 2006, but that Groups VIII to XIII will be rejoined, one to the other as drawn to a method for assessing the activity of fibrosis stimulating signal in hepatic fibrosis and the efficacy of the molecular targeting therapy for hepatic-fibrosis, but will remain restricted to three Groups of methods using antibodies specific for the phosphorylated linker region in Smad2, Smad3, or Smad2 and Smad3. In particular, examiner stated in response to applicant's arguments "that there is no difference in the steps of claim 11"

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corresponding to the two purposes that "the groups" (clearly referring of course to Groups VIII to XIII) will be rejoined. Although section 5 also refers to the maintenance of the restriction to three groups of methods using antibodies specific for the three sets of proteins claimed, this is specifically in reference to the restriction requirements already set forth in groups VIII to XIII at pages 4 and 5 of the restriction requirement.

Thus for the reasons set forth previously and above, the restriction requirement is deemed to be proper and is maintained as FINAL.

4 Claims 1-5, 13 and 14 are currently being examined.

Priority

5. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Japan on October 10, 2003, App. No. 2003-351259 and receipt of the certified copy of the Japanese Application.

It is noted that examiner maintains the priority date of April 13, 2004, because the priority of the instantly claimed invention is based on the Japanese patent App. No. 2003-351259, which has not been translated and Examiner is unable to determine the information in the document. If Applicant disagrees with any rejection set forth in this action based on examiner's establishment of a priority date of April 13, 2004 for the instantly claimed application serial number 10/822,860, applicant is invited to submit a proper translation of the priority document and to point to page and line where support can be found establishing an earlier priority date. If applicant chooses to file a translation, then the translation must be filed together with a statement that the translation of the certified copy is accurate, see MPEP 201.15.

Title

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6. The title of the invention is not descriptive as previously indicated in the Office Action of December 14, 2006. Given that the restriction is final, a title such as "Antibodies to the phosphorylated linker region of Smad 2 and Smad 3" is suggested.

Response to Amendment

7. The Declaration under 37 CFR 1.132 filed March 9, 2007 is sufficient to overcome the rejection of claims 1, 2, 4, and 5 based upon Furukawa et al. (Hepatology, September 27, 2003, 38:879-889).

New Grounds of Rejection

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 1, 2, 4 and 5 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Kretschmar et al. (Genes & Development, 1999, 13:804-816, IDS item), in further view of Socuhelnytokyi et al. (US Patents 6,103,869), and further in view Harlow and Lane (Antibodies, a Laboratory Manual, Cold Spring Harbor Laboratory Press, 1988, p. 93-94 and p.142, previously cited).

The claims are drawn to 1. An affinity-purified polyclonal antibody specific for a phosphorylated linker region in Smad2 and/or Smad3; 2. A polyclonal antibody specific for a phosphorylated linker region in Smad2 and/or Smad3, obtained from antiserum raised by immunizing a mammal with a phosphorylated product of a peptide including an amino acid sequence in the linker region of Smad2 or Smad3. 4. The polyclonal antibody according to claim 2, wherein the mammal is a rabbit; 5. The polyclonal antibody to claim 2, wherein the raised antiserum is affinity purified with a phosphorylated peptide(s)

Kretzschmar et al. teach an isolated recombinant Smad 2 and Smad 3 that are directly phosphorylated in the linker region by Erk 2 and these phosphorylations are stimulated by Epidermal Growth Factor and the activated oncogene RasV12, see p. 807-right column, p. 808-left column, and Fig. 5. Kretzschmar et al. teach that Ras induced phosphorylation of Smad2 and Smad3 in the linker region inhibits the nuclear accumulation of the Smads and their ability to mediate Transforming Growth Factor Beta antiproliferative responses in cancer cells, see p.810, right column and Abstract.

Kretzschmar et al teach as set forth above, but do not teach polyclonal antibodies raised in a mammal to the phosphorylated linker region in Smad2 and/or Smad 3.

Socuhelnytokyi et al teach that antisera to phosphorylated pathway-restricted Smad proteins which cross react with nonphosphorylated pathway-restricted Smad proteins can be affinity purified, if desired, to obtain polyclonal antibodies which recognize only phosphorylated pathway-restricted Smad proteins, see col. 33, lines 55-60.

Additionally, Harlow and Lane teach that, although in theory monoclonal antibodies can be used for all of the tasks for which polyclonal antibodies are used, in practice one cannot predict how a monoclonal antibody will function, see p. 142, first para., and Table 6.1. Further, Harlow and Lane teach that “. . . producing exactly the right set of monoclonal antibodies is often a difficult and laborious job,.” (p. 142, first para).

Harlow and Lane teach the five commonly used laboratory animals for the production of antisera are the mammals rabbits mice, rats, hamster, and guinea pigs, see p. 93 and Table 5.2. Harlow and Lane further teach that rabbits represent a good choice for the routine production of polyclonal antibodies because they are easy to keep and handle, can be safely and repeatedly

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bled, and the antibodies they produce are well characterized and easily purified, see p.92 and Table 5.2.

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to have produced antibodies to the well known phosphorylated SMAD2 and/or 3 because the Board of Patent Appeals and interferences has taken the position that once an antigen has been isolated, the manufacture of antibodies against it is *prima facie* obvious. See *Ex parte Erlich*, 3 USPQ 2d 1011 (PTO Bd. Pat. APP. & Int. 1986).

Further, one would have been motivated to make polyclonal antibodies to the phosphorylated SMAD2 and/or 3 because Kretzschmar et al. shows the proteins in two different phosphorylation states and it would be useful to have antibodies that differentiate between phosphorylated and unphosphorylated SMAD2 and/or 3. Given that the phosphorylation of SMAD-2 and SMAD-3 in the linker region is regulated by a known oncogene, Ras, it would have been *prima facie* obvious to one of skill in the art to make polyclonal antibodies to these phosphorylated sites in the linker of Smad-2 and/or Smad-3 because of the importance understanding cellular mechanisms related to cancer. Further, it would have been expected that at least a subset of the polyclonal antibodies produced would be specific for a phosphorylated linker region of either SMAD2 and/or 3.

Further, it would have been *prima facie* obvious and one would have been motivated to produce polyclonal antibodies to the well known phosphorylated SMAD2 and/or 3 because Harlow et al specifically teach that monoclonal antibodies are often more time-consuming and costly to prepare and they are not necessarily the best choice for certain immunochemical techniques. Although in theory, monoclonal antibodies can be used for all of the tasks that

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require or benefit from the use of polyclonal antibodies, in practice, producing exactly the right set of monoclonal antibodies is often a difficult and laborious job and polyclonal antibodies are useful for cell staining, immunoprecipitation and immunoblot techniques. Given the conventional nature of the production of polyclonal antibodies at the time the invention was made, one would have had a reasonable expectation of successfully producing polyclonal antibodies to phosphorylated SMAD2 and/or 3

Further, it would have been prima facie obvious and one would have been motivated to produce affinity purified polyclonal antibodies because Socuhelnytokyi et al teach affinity purification can be used to obtain polyclonal antibodies which recognize only phosphorylated pathway-restricted Smad proteins. Thus, the increased specificity of affinity purified polyclonal antibodies would have motivated one of ordinary skill in the art to purify the polyclonal antibodies with a phosphorylated peptide to improve the specificity of the polyclonal antibodies generated. Furthermore, given that affinity purification was a routinely performed art technique at the time the invention was made, one of skill in the art would have had a reasonable expectation of success of affinity purifying the polyclonal antibodies.

Furthermore, the prior art teaches that mammals are routinely used for polyclonal antibody production and rabbits have numerous advantages for the production of polyclonal antibodies. Given that mammals are routinely used for polyclonal antibody production and rabbits have numerous advantages for the production of polyclonal antibodies, one of skill in the art at the time the invention was made would have had a reasonable expectation of success of making the polyclonal antibodies in a mammal.

Thus one of ordinary skill in the art would have had motivation and a reasonable expectation of success in making and using the claimed invention for the reasons above.

Some of Applicant's arguments in the remarks of March 9, 2007 are germane to the instant rejection.

Applicant argues that the issue in the rejection is, given that the phosphorylated linker regions of Smad2 and Smad3 are known, whether any antibodies directed against these regions would be obvious. Applicant argues that Ex parte Erlich is discussed in MPEP 2143.02. Applicant argues that in MPEP 2143.02, the case is discussed with regard to predictability in the art, motivation, and expectation of success, and the MPEP emphasizes that the wording in the decision specifically uses the wording "in this case" and "this invention," that is, emphasizes that the decision is very specific to the facts in that particular case. Applicant argues that the Examiner is improperly broadly interpreting the decision in Ex parte Erlich, and that the decision in that case does not generally state that "once an antigen has been isolated, the manufacture of antibodies ...against it is prima facie obvious," as the Examiner contends on page 10, lines 18-20. (Applicant cannot find such a statement in the text of the decision).

Applicant argues that the main issue in Ex parte Erlich appears to be an issue of unpredictability raised by Erlich, which the Board considered not to interfere with the "reasonable expectation of success." Applicant argues that however, the contention of the Examiner appears to be that there is a suggestion or motivation in the general art to prepare antibodies against any known protein. Applicant argues that the issue does not even appear to have been addressed in Ex parte Erlich.

Applicant argues that in general with regard to obviousness, MPEP 2143.01 states:
"Obviousness can only be established by combining or modifying the teachings of the

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prior art to produce the claimed invention where there is some teaching, suggestion or motivation to do so found either in the references themselves or in the knowledge generally available to one of ordinary skill in the art."

MPEP 2142 provides:

"To establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. Second, there must be a reasonable expectation of success. Finally, the prior art reference (or references when combined) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art, and not based on applicant's disclosure."

Applicant argues that there cannot be considered to be a teaching in the general art to prepare an antibody against every known protein. Applicant argues that if there were, every conceivable antibody would be automatically prima facie obvious

Applicant's arguments have been carefully considered, but have not been found persuasive. In regard to the use of the wording "in this case" and "this invention," the Board is referring to a previous decision, *Exparte Old*, 229 USPQ 196 (PTO Bd. App. and Inter. 1985), that had reversed the rejection before it, finding a degree of unpredictability in the use of malignant human renal cells as the antigenic determinant for making monoclonal antibodies. However, in regard to the obviousness of making monoclonal antibodies to human fibroblast interferon, the Board states, "Here, we have no doubt that, in view of the facts of record *in this case* at the time *this* invention was made, one of ordinary skill in the art would have been motivated to produce monoclonal antibodies specific for human fibroblast interferon using the method of Kohler and Milstein with a reasonable expectation of success". Furthermore, the

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board states that "From our analysis, we find that it would have been obvious to one of ordinary skill in the art at the time the present invention was made to use the basic method of Kohler and Milstein to form monoclonal antibodies specific for human fibroblast interferon since human fibroblast interferon was a known antigen of unquestioned research interest as an antiviral or antitumor agent." Thus, at the time of the Erlich decision it was obvious to make monoclonal antibodies to antigens of unquestioned research interest. It is noted that antibodies for a phosphorylated linker regions in SMAD2 and/or SMAD 3 are of unquestioned research interest for the reasons set forth previously an above, thus the findings set forth in Ex parte Erlich are clearly applicable to the instant case. Although, Erlich does not directly speak to making polyclonal antibodies, the process of making polyclonal antibodies involves the first step of the cited Kohler and Milstein method, injecting the antigen into an animal, and then collecting serum that contains the polyclonal antibody. Given that the phosphorylation of SMAD-2 and SMAD-3 in the linker region is regulated by a known oncogene, Ras, given that there is a well known interest in the art in understanding the mechanism of regulation of cancer cells, given that making polyclonal antibodies was conventional at the time the invention was made, and given that polyclonal antibodies perform some research function better than monoclonal antibodies, it would have been *prima facie* obvious to one of skill in the art at the time the invention was made to make polyclonal antibodies to the phosphorylated linker region of Smad-2 or Smad-3.

Applicant argues that the issue here is whether there is some teaching, suggestion or motivation in Kretzschmar et al., in Harlow and Lane, or in the general art, to prepare an antibody against the phosphorylated Smad2 or Smad3 of Kretzschmar. Applicant argues that there is no such suggestion in Harlow and Lane. Applicant argues that with regard to

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Kretzschmar, this reference notes that TGF β 3 exerts growth inhibitory and transcriptional responses through Smad2 and Smad3 (page 804, column 2), stating that these are TGF β 3 substrate receptors. The reference studied Ras-induced phosphorylation of Smad2 and Smad3 linker regions (p. 807, column 2), showing that these were phosphorylated under normal culture conditions, and increased by transfection with H-Ras. "The results suggest that the basal activity of the Ras pathway and, to a larger extent, the hyperactivation of this pathway by H-Ras or activated Mek I, cause the phosphorylation of Smad2 and Smad3."

Applicant argues that the phosphorylation studies in the reference have been mainly carried out using ^{32}P -labeling and Western immunoblotting or immunoprecipitation. The anti-Smad2 and anti-Smad3 antibodies used appear to be generic antibodies not directed against the phosphorylated linker region. Applicant also submits that these anti-Smad antibodies were completely adequate for detecting phosphorylated Smad2 and Smad3 in Kretzschmar's Western blotting and immunoprecipitation studies, and therefore there appears to be no suggestion in Kretzschmar to prepare any other antibodies, in particular antibodies against the phosphorylated linker regions, in order to analyze these proteins.

Applicant argues that in the summary of Kretzschmar on page 812, column 2, the reference discusses the nuclear accumulation of Smad2/Smad3. However, the reference is only an investigation into this phenomenon, and this provides no suggestion or motivation for antibodies against the phosphorylated linker region of Smad2 or Smad3.

Applicant's arguments have been carefully considered, but have not found persuasive because Applicant has argued and discussed the references individually without clearly addressing the combined teachings. It must be remembered that the references are relied upon in

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combination and are not meant to be considered separately as in a vacuum. It is the combination of all of the cited and relied upon references which made up the state of the art with regard to the claimed invention. Applicant's claimed invention fails to patentably distinguish over the state of the art represented by the cited references taken in combination. In re Young, 403 F.2d 754, 159 USPQ 725 (CCPA 1968); In re Keller 642 F.2d 413, 208 USPQ 871 (CCPA 1981). For the reasons set forth above, one of skill in the art would have been motivated and would have had a reasonable expectation of success to make affinity purified polyclonal antibodies to the phosphorylated linker region of SMAD2 and/or SMAD 3.

Claim Objections

10. Claims 3, 13 and 14 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
11. All other objections and rejections recited in October 11, 2006 are withdrawn.
12. No claims allowed.
13. This action is a **final rejection** and is intended to close the prosecution of this application. Applicant's reply under 37 CFR 1.113 to this action is limited either to an appeal to the Board of Patent Appeals and Interferences or to an amendment complying with the requirements set forth below.

If applicant should desire to appeal any rejection made by the examiner, a Notice of Appeal must be filed within the period for reply identifying the rejected claim or claims appealed. The Notice of Appeal must be accompanied by the required appeal fee.

If applicant should desire to file an amendment, entry of a proposed amendment after final rejection cannot be made as a matter of right unless it merely cancels claims or complies with a formal requirement made earlier. Amendments touching the merits of the application which otherwise might not be proper may be admitted upon a showing a good and sufficient reasons why they are necessary and why they were not presented earlier.

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A reply under 37 CFR 1.113 to a final rejection must include the appeal form, or cancellation of, each rejected claim. The filing of an amendment after final rejection, whether or not it is entered, does not stop the running of the statutory period for reply to the final rejection unless the examiner holds the claims to be in condition for allowance. Accordingly, if a Notice of Appeal has not been filed properly within the period for reply, or any extension of this period obtained under either 37 CFR 1.136(a) or (b), the application will become abandoned.

14. Applicant's amendment necessitated the new grounds of rejection. Thus, **THIS ACTION IS MADE FINAL**. Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. ' 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. ' 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Peter J. Reddig whose telephone number is (571) 272-9031. The examiner can normally be reached on M-F 8:30 a.m.-5:00 p.m..

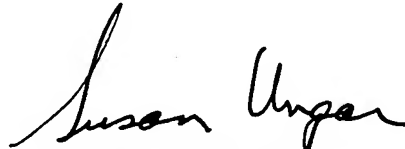
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on (571) 272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR

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system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Peter J. Reddig, Ph.D.
Examiner
Art Unit 1642



SUSAN UNGAR, PH.D.
PRIMARY EXAMINER

PJR